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EXAMINER
CARLSON, K

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ART UNIT	PAPER NUMBER
1812	4

DATE MAILED: 08/28/92

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), — days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice re Patent Drawing, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-18, 22, 23 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☒ Claims 19-21, 24-26 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-18, 22, 23 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☒ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☒ been received ☐ not been received ☐ been filed in parent application, serial no. 07/511,430; filed on 4-20-90
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

PTOL-326 (Rev. 9-89)

EXAMINER'S ACTION

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Claims 1-18, 22, and 23 are pending in this application. Claims 19-21 and 24-26 have been cancelled by the applicants in Paper #2, filed February 11, 1992.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure.

The Applicants have incorporated several references into the specification. For example, Adelman et al. on page 15. Mere

reference to another application, patent, or publication is not an incorporation of anything therein into the application containing such reference for purposes of disclosure required by 35 USC 112 (In re de Seversky 177 USPQ 144). Therein, essential material that the Applicants may want expressly in the specification should be written in the specification and not referred to in this manner.

The specification does not enable the ability of "variants" of the TNF-binding protein or receptor to bind to TNF. There are a multitude of different substitutions, deletions, and insertions into the TNF binding protein or receptor that are loosely discussed in the specification. Those sequences which the applicants envision as part of their invention should be shown to have appropriate activity.

Claims 1-18, 22, and 23 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 1-18 and 23 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 2, 8, 9, 13, and 23 claim undisclosed fragments, degenerate variants, or functional derivatives of the TNF receptor protein. These sequences are not particularly pointed out and therefore do not expressly state what the Applicants intend to claim. Claim 7 does not describe

the precise conditions by which the hybridization of the nucleic acids will occur; therein, this claim is vague and indefinite. Claims 11-16 refer to plasmids containing the TNF receptor or binding protein cDNA. These plasmids have not been deposited and are not described in the claims in such a manner that clearly describes what the Applicants view as their invention. If the plasmids have been deposited, then the accession number should be included in the claim.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-18, 22 and 23 are rejected under 35 U.S.C. § 103 as obvious over Wallach et al. (EPA 0308378; published March 22, 1989). Wallach et al. teach the purification (page 6) of TNF-BP from urine. The TNF-BP was characterized by its ability to

inhibit TNF receptor binding (page 5) and as having an N-terminal amino acid sequence as follows (page 8):

Asn-Ser-Val-Cys-Pro-Gln-Gly-Lys-Tyr-Ile-His-Pro-Gln-X-Asn-Ser

This partial sequence is encoded by the DNA that is disclosed by the Applicants. Wallach et al. used antibodies against TNF-BP to search for cells producing TNF-BP by immunofluorescence or western blot analysis (page 8). They then prepared a cDNA encoding TNF-BP in TNF-BP producing cells by extracting the mRNA from the cells, reverse transcribing the mRNA to acquire the cDNA, cloning the cDNA, and screening the cDNA library by using antibody probes (page 8-9). Wallach et al. go on to describe two other methods by which to acquire the cDNA from the known protein sequence as described above. Transcriptional promoters, enhancers, and terminators for eukaryotic expression of the DNA is also taught (page 10). Wallach et al. do not expressly teach the DNA sequence encoding the TNF receptor or binding protein nor the claimed plasmids. However, this reference makes the invention claimed by the Applicants obvious because knowing the partial protein sequence, one of ordinary skill in the art can readily isolate the DNA encoding the protein because this isolation is taught by Wallach et al. Wallach et al. clearly teaches how to make the antibodies against the TNF-BP, isolate the mRNA from appropriate cells, acquire the cDNA, and screen the cDNA library for the clone containing the gene for TNF-BP (Claims 1-10). Wallach et al. teach the insertion of the cDNA into vectors and the expression of this cDNA from eukaryotic cells

(Claims 11-18, 22, 23). Therefore, all pending claims are rejected under ~~35 USC 102 or~~ 35 USC 103, because this invention has been taught or is obvious in view of Wallach et al.

Claims 1-18, 22, and 23 are rejected under 35 U.S.C. § 103 as being unpatentable over the combined teachings of Olsson et al. (March, 1989) and Clark et al. (US Patent 4,675,285; 1987). Olsson et al. teach the isolation (page 271) and characterization of TNF-BP from urine. They were able to show that this binding protein was approximately 30kD (Fig. 3) and that the N-terminal amino acid sequence was (page 274):

Asn-Ser-Val-Xxx-Pro-Gln-Gly-Lys-Tyr-Ile-His-Pro-Gln-Val-Asn-Ser-Ile-Xxx-Lys-Thr

This partial sequence is encoded by the DNA that is disclosed by the Applicants. Fig. 1 shows that this isolated protein bound to TNF as demonstrated by affinity chromatography. This TNF-BP was purified and characterized to such an extent that even the amino acid composition of the binding protein was analyzed (Fig. 2). Olsson et al. conclude that "it is important to consider the possibility that TNF-BP may be a soluble form of the TNF receptor" (page 275). Olsson et al. do not expressly teach the DNA sequences or the plasmids claimed by the Applicants. None-the-less, with this partial consecutive amino acid sequence known and the motivation to isolate the receptor for and the binding protein to TNF, one of ordinary skill in the art could use the teachings of Clark et al. to isolate the DNA encoding the

protein. Clark et al. teaches a method of isolating DNA encoding a known protein which entails identifying cells that produce the protein, isolating the mRNA from the cells, reverse transcribing the mRNA to cDNA (column 14), and inserting the cut cDNA into an expression vectors (column 15), and transforming E. coli to express the DNAs(column 15). The clone that contained the DNA encoding the desired protein was identified by assaying the culture media for protein activity (column 17). Clark et al. do not teach this method for the isolation of DNA encoding the TNF receptor or binding protein but this is described as a universal method in which the DNA encoding a known protein can be isolated. Therein, taken together, it would have been obvious to one of ordinary skill in the art at the time the invention was made to identify cells that have receptors to TNF, isolate mRNA from the cells, reverse transcribe the mRNA to cDNA, clone the cDNA, and identify the clone containing the cDNA by using a binding assay for TNF because Olsson et al. have isolated and characterized the soluble TNF-BP and suggest that the soluble TNF-BP may be a part of the TNF receptor itself and Clark et al. teach that this method can be used in a universal manner to isolate DNA that encodes a protein of interest. Therefore, Claims 1-18, 22, and 23 are obvious in view of the prior art.

Any inquiry concerning this communication should be directed to Karen Cochrane Carlson, Ph.D. at telephone number (703) 305-7811.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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